The structural and biomechanical properties of insect thick filaments expressing flightin and cardiac myosin binding protein-C

Abstract

The purpose of this study is to examine the hypothesis that Cardiac Myosin Binding Protein-C (cMyBP-C) is a vertebrate functional homolog to invertebrate Flightin (FLN), both found in their corresponding organism's muscle thick filament. We generated four *D. melanogaster* mutant and transgenic strains used in this study: FLN knockout strain (fln^0), a knockout rescued transgenic strain (fln^0;fln^+), a transgenic cMyBP-C strain without FLN expression (fln^0 $MyBPC^+$), and a transgenic strain with FLN expression alongside cMyBP-C expression (fln^+ $MyBPC^+$). To test the hypothesis that FLN and cMyBP-C are functionally homologous, we determined the extent to which cMyBP-C can rescue the phenotype engendered by fln^0. By Transmission Electron Microscopy (TEM), we gathered data on the structural characteristics of the flight muscle sarcomeres of the *Drosophila* strains. The results attained from TEM confirmed both the sarcomere length measurements and level of structural order previously seen for fln^0 and fln^+, while revealing excessive shortening of the sarcomere in the transgenic lines involving cMyBP-C alone. Atomic Force Microscopy (AFM) was used to collect data on the mechanical properties of isolated, native thick filaments. It was shown that persistence length (PL) for fln^+ $MyBPC^+$ was significantly higher (2.6µm vs. 1.7µm; $p<0.005$) than PL for fln^+ despite the similarity between them in sarcomere structure by TEM. PL for fln^0 and fln^0 $MyBPC^+$ grouped close together within a mean range of 0.71-1.2µm. We concluded that ectopically expressed cMyBP-C can influence sarcomere length and thick filament stiffness in the flight muscle, consistent with the hypothesis that cMyBP-C and FLN may have convergent functions. This brings us closer to understanding the role of myosin binding proteins in dictating the structural and mechanical properties of thick filaments, an important determinant of muscle functional properties.